

AMENDMENTS TO THE CLAIMS

1-55 (canceled).

56. (new) A method of making a modified hepadnavirus core antigen comprising:
providing a first nucleic acid encoding a heterologous antigen;
providing a second nucleic acid encoding a hepadnavirus core antigen;
determining the isoelectric point of said heterologous antigen encoded by said first
nucleic acid and, if said heterologous antigen is determined to have an isoelectric point greater
than or equal to 7.0, adding nucleotides that encode an acidic amino acid to said first nucleic acid
to reduce said isoelectric point below 7.0;

combining said first and second nucleic acids; and
expressing said first and second nucleic acids to produce a modified hepadnavirus core
antigen comprising the amino acids encoded by said first and second nucleic acids.

57. (new) The method of Claim 56, wherein in the absence of said adding nucleotides,
expression of said modified hepadnavirus core antigen yields 25 fold or less particles than does
expression of a wild type hepadnavirus core antigen.

58. (new) The method of Claim 56, wherein after adding nucleotides to said first nucleic
acid, said heterologous antigen encoded by said first nucleic acid is determined to have an
isoelectric point in the range of 3.0 - 5.0.

59. (new) The method of Claim 56, wherein said adding nucleotides that encode an
acidic amino acid results in a substitution of a non-acidic amino acid residue within said
heterologous antigen, with said acidic amino acid residue.

60. (new) The method of Claim 59, wherein said non-acidic amino acid residue is a basic
amino acid residue.

61. (new) The method of Claim 56, wherein said adding nucleotides that encode an acidic amino acid results in an insertion of said acidic amino acid residue.
62. (new) The method of Claim 61, wherein said adding nucleotides that encode an acidic amino acid results in at least one acidic amino acid that flanks said heterologous antigen.
63. (new) The method of Claim 62, wherein said acidic amino acid is a linker that flanks both sides of said heterologous antigen.
64. (new) The method of Claim 56, wherein said hepadnavirus core antigen is a truncated hepadnavirus core antigen.
65. (new) The method of Claim 56, wherein said hepadnavirus core antigen comprises an artificial C-terminus.
66. (new) The method of Claim 56, wherein said hepadnavirus core antigen is a truncated hepadnavirus core antigen comprising an artificial C-terminus.
67. (new) The method of Claim 56, wherein said hepadnavirus core antigen is a woodchuck hepadnavirus core antigen.
68. (new) The method of Claim 56, wherein said hepadnavirus core antigen is a human hepadnavirus core antigen.

69. (new) A method of making a modified hepadnavirus core antigen comprising:
providing a first nucleic acid encoding a heterologous antigen;
providing a second nucleic acid encoding a hepadnavirus core antigen;
determining the isoelectric point of said heterologous antigen encoded by said first
nucleic acid and, if said heterologous antigen is determined to have an isoelectric point greater
than or equal to 7.0, adding nucleotides that encode an acidic amino acid to said second nucleic
acid at a position within an immunodominant loop of said hepadnavirus core antigen or within an
alpha-helix adjacent to said immunodominant loop;
combining said first and second nucleic acids; and
expressing said first and second nucleic acids to produce a modified hepadnavirus core
antigen comprising the amino acids encoded by said first and second nucleic acids.

70. (new) The method of Claim 69, wherein in the absence of said adding nucleotides,
expression of said modified hepadnavirus core antigen yields 25 fold or less particles than does
expression of a wild type hepadnavirus core antigen.

71. (new) The method of Claim 69, wherein said combining comprises placing said first
and second nucleic acids in operable combination such that said heterologous antigen is
expressed within said immunodominant loop or said alpha-helix adjacent to said
immunodominant loop.

72. (new) The method of Claim 71, wherein said position is within said
immunodominant loop of said hepadnavirus core antigen

73. (new) The method of Claim 71, wherein said position is within said alpha-helix
adjacent to said immunodominant loop.

74. (new) The method of Claim 71, wherein said adding nucleotides that encode an
acidic amino acid results in a substitution of a non-acidic amino acid residue within said
hepadnavirus core antigen, with said acidic amino acid residue.

75. (new) The method of Claim 74, wherein said non-acidic amino acid residue is a basic amino acid residue.

76. (new) The method of Claim 71, wherein said adding nucleotides that encode an acidic amino acid results in an insertion of said acidic amino acid residue.

77. (new) The method of Claim 76, wherein said adding nucleotides that encode an acidic amino acid results in at least one acidic amino acid within said immunodominant loop of said hepadnavirus core antigen.

78. (new) The method of Claim 76, wherein said adding nucleotides that encode an acidic amino acid results in at least one acidic amino acid within said alpha helix adjacent to said immunodominant loop.

79. (new) The method of Claim 76, wherein said adding nucleotides that encode an acidic amino acid results in at least one acidic amino acid that flanks said heterologous antigen.

80. (new) The method of Claim 79, wherein said acidic amino acid is a linker that flanks both sides of said heterologous antigen.

81. (new) The method of Claim 71, wherein said hepadnavirus core antigen is a truncated hepadnavirus core antigen.

82. (new) The method of Claim 71, wherein said hepadnavirus core antigen comprises an artificial C-terminus.

83. (new) The method of Claim 71, wherein said hepadnavirus core antigen is a truncated hepadnavirus core antigen comprising an artificial C-terminus.

84. (new) The method of Claim 71, wherein said hepadnavirus core antigen is a woodchuck hepadnavirus core antigen.

85. (new) The method of Claim 71, wherein said hepadnavirus core antigen is a human hepadnavirus core antigen.

86. (new) The method of Claim 56, wherein said expression of said first and said second nucleic acids is in a bacterial cell.

87. (new) The method of Claim 56, wherein said expression of said first and said second nucleic acids is in a mammalian cell.

88. (new) The method of Claim 69, wherein said expression of said first and said second nucleic acids is in a bacterial cell.

89. (new) The method of Claim 69, wherein said expression of said first and said second nucleic acids is in a mammalian cell.

90. (new) A method of making a nucleic acid that encodes a modified hepadnavirus core antigen comprising:

providing a first nucleic acid encoding a heterologous antigen;

providing a second nucleic acid encoding a hepadnavirus core antigen;

determining the isoelectric point of said heterologous antigen encoded by said first nucleic acid and, if said heterologous antigen is determined to have an isoelectric point greater than or equal to 7.0, adding nucleotides that encode an acidic amino acid to said first nucleic acid to reduce said isoelectric point below 7.0; and

combining said first and second nucleic acids so as to produce said nucleic acid that encodes said modified hepadnavirus core antigen.

91. (new) The method of Claim 90, wherein after adding nucleotides, said heterologous antigen is determined to have an isoelectric point in the range of 3.0 - 5.0.

92. (new) The method of Claim 90, wherein said adding nucleotides that encode an acidic amino acid results in a substitution of a non-acidic amino acid residue within said heterologous antigen, with said acidic amino acid residue.

93. (new) The method of Claim 90, wherein said non-acidic amino acid residue is a basic amino acid residue.

94. (new) The method of Claim 90, wherein said adding nucleotides that encode an acidic amino acid results in an insertion of said acidic amino acid residue.

95. (new) The method of Claim 94, wherein said adding nucleotides that encode an acidic amino acid results in at least one acidic amino acid that flanks said heterologous antigen.

96. (new) The method of Claim 95, wherein said acidic amino acid is a linker that flanks both sides of said heterologous antigen.

97. (new) The method of Claim 90, wherein said hepadnavirus core antigen is a truncated hepadnavirus core antigen.

98. (new) The method of Claim 90, wherein said hepadnavirus core antigen comprises an artificial C-terminus.

99. (new) The method of Claim 90, wherein said hepadnavirus core antigen is a truncated hepadnavirus core antigen comprising an artificial C-terminus.

100. (new) The method of Claim 90, wherein said hepadnavirus core antigen is a woodchuck hepadnavirus core antigen.

101. (new) The method of Claim 90, wherein said hepadnavirus core antigen is a human hepadnavirus core antigen.

102. (new) A method of making a nucleic acid that encodes a modified hepadnavirus core antigen comprising:

providing a first nucleic acid encoding a heterologous antigen;

providing a second nucleic acid encoding a hepadnavirus core antigen;

determining the isoelectric point of said heterologous antigen encoded by said first nucleic acid and, if said heterologous antigen is determined to have an isoelectric point greater than or equal to 7.0, adding nucleotides that encode an acidic amino acid to said second nucleic acid at a position within an immunodominant loop of said hepadnavirus core antigen or within an alpha-helix adjacent to said immunodominant loop; and

combining said first and second nucleic acids so as to produce said nucleic acid that encodes said modified hepadnavirus core antigen.

103. (new) The method of Claim 102, wherein said combining comprises placing said first and second nucleic acids in operable combination such that said heterologous antigen is expressed within said immunodominant loop or said alpha-helix adjacent to said immunodominant loop.

104. (new) The method of Claim 102, wherein said position is within said immunodominant loop of said hepadnavirus core antigen

105. (new) The method of Claim 102, wherein said position is within said alpha-helix adjacent to said immunodominant loop.

106. (new) The method of Claim 102, wherein said adding nucleotides that encode an acidic amino acid results in a substitution of a non-acidic amino acid residue within said hepadnavirus core antigen, with said acidic amino acid residue.

107. (new) The method of Claim 106, wherein said non-acidic amino acid residue is a basic amino acid residue.

108. (new) The method of Claim 102, wherein said adding nucleotides that encode an acidic amino acid results in an insertion of said acidic amino acid residue.

109. (new) The method of Claim 108, wherein said adding nucleotides that encode an acidic amino acid results in at least one acidic amino acid within said immunodominant loop of said hepadnavirus core antigen.

110. (new) The method of Claim 108, wherein said adding nucleotides that encode an acidic amino acid results in at least one acidic amino acid within said alpha helix adjacent to said immunodominant loop.

111. (new) The method of Claim 108, wherein said adding nucleotides that encode an acidic amino acid results in at least one acidic amino acid that flanks said heterologous antigen.

112. (new) The method of Claim 111, wherein said acidic amino acid is a linker that flanks both sides of said heterologous antigen.

113. (new) The method of Claim 102, wherein said hepadnavirus core antigen is a truncated hepadnavirus core antigen.

114. (new) The method of Claim 102, wherein said hepadnavirus core antigen comprises an artificial C-terminus.

115. (new) The method of Claim 102, wherein said hepadnavirus core antigen is a truncated hepadnavirus core antigen comprising an artificial C-terminus.

116. (new) The method of Claim 102, wherein said hepadnavirus core antigen is a woodchuck hepadnavirus core antigen.